

AMENDMENTS TO THE CLAIMS

1. (Currently amended) An isolated human cytokine-binding domain structure of Domain 4 of a β_c chain of a cytokine receptor which binds to at least one cytokine and is capable of transducing a cytokine signal through a single cytokine receptor, said domain ~~comprising a region defined by an N terminus of Domain 4 and by a B'-C' loop, said B'-C' loop including residues Tyr365, His367, and Ile368 of Domain 4 of the β_c chain consisting of a portion of D4 β_c said portion defined by a portion of the B'-C' loop of D4 β_c and a groove defined by the B'-C', F'-G' loops and the N-terminal section of D4 β_c and having a surface representation and alignment to a structure according to Figure 1.~~
2. (Currently amended) The cytokine-binding domain structure according to claim 1 ~~comprising the B'-C' loop of Domain 4 and a groove which is defined by the B'-C', F'-G' loops, and wherein the F'-G' loop comprises residues 418 and 421 of Domain 4 of the β_c chain, and the N-terminal section of Domain 4.~~
3. (Canceled)
4. (Currently amended) The cytokine-binding domain structure according to claim 3 1 including a Tyrosine residue capable of interaction with an α chain subunit or with Domain 3 of the β_c chain subunit to allow high affinity binding of the cytokine wherein the tyrosine is Tyr421.
5. (Currently amended) The cytokine-binding domain structure according to claim 1 wherein the B'-C' loop residues of Domain 4 of the β_c chain form a type 1 β -turn.
6. (Currently amended) The cytokine-binding domain structure according to claim 1 wherein the binding domain of the β_c chain, which binds to at least one cytokine, is defined by an area bordered by any one of the following residues including selected from the group consisting of Lys362, Tyr365, His367, Ile368, Arg418, Gly420, Asn422, Thr416, Ile338, Gln339, Met340 and Met361 or combination thereof.

7. (Canceled)

8. (Currently amended) The cytokine-binding domain structure according to claim 1 that binds to at least two cytokines selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13.

9. (Canceled)

10. (Currently amended) The cytokine-binding domain structure according to claim 9 1 wherein the β_c chain ~~is derived from a~~ of the receptor ~~is~~ selected from the group consisting of IL-5 receptor, IL-3 receptor and GM-CSF receptor.

11. (Currently amended) The cytokine-binding domain structure according to claim 2 wherein the F'-G' loop adopts a type IV β -turn.

12. (Withdrawn) A method of identifying a compound having cytokine agonist or antagonist activity which comprises:

subjecting a potential cytokine agonist and/or cytokine antagonist compound to the cytokine binding domain according to claim 1; and

determining the presence of an agonist or antagonist response to the compound on the activity of a cytokine.

13. (Withdrawn) A method of identifying a compound having a cytokine agonist or antagonist activity, which comprises:

subjecting a potential cytokine antagonist to the cytokine binding domain-according to claim 1; and

identifying a compound that has bound to the cytokine-binding domain wherein said compound has an agonist or antagonist response on the activity of the cytokine.

14. (Withdrawn) The method according to claim 12 wherein the cytokine is selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13; and the presence of an agonist or antagonist is determined by the ability of the agonist or antagonist to activate or inhibit an IL-3, IL-5, GM-CSF, IL-4, or IL-13 response.

15. (Withdrawn) The method according to claim 12 wherein the cytokine agonist or antagonist further binds to Tyr421 of a cytokine receptor.

16. (Withdrawn) A cytokine agonist or antagonist identified by a method according to claim 12.

17. (Withdrawn) An antibody or fragment thereof to the cytokine binding domain according to claim 1.

18. (Withdrawn) The cytokine binding domain according to claim 1 comprising a mutation directed to a residue selected from a group consisting of Gln340, Ile338 and Met361 of Domain 4 of the β_c chain.

19. (Withdrawn) A method of preventing or treating a cytokine-related condition, which method comprises administering to a subject an effective amount of an agonist or antagonist according to claim 16.

20. (Withdrawn) A method of preventing or treating a cytokine-related condition, which method comprises administering to a subject an effective amount of an antibody according to claim 17.

21. (Withdrawn) The method according to claim 19 wherein the cytokine-related condition is selected from the group including survival or activation of eosinophil function, asthma,

leukemia, breast cancer, prostate cancer, small cell lung carcinoma, colon cancer, chronic inflammation including rheumatoid arthritis, immunosuppression, allergy, lymphoma, and cachexia, and wherein said cytokine agonist or antagonist is an antagonist.

22. (Withdrawn) The method according to claim 20 wherein the cytokine-related condition is selected from the group including survival or activation of eosinophil function, asthma, leukemia, breast cancer, prostate cancer, small cell lung carcinoma, colon cancer, chronic inflammation including rheumatoid arthritis, immunosuppression, allergy, lymphoma, and cachexia.

23. (Withdrawn) The method according to claim 19 wherein the cytokine-related condition is allergic inflammation and the antagonist inhibits the binding of IL-5, IL-3 or GM-CSF to the IL-5, IL-3 or GM-CSF receptor.

24. (Withdrawn) The method according to claim 20 wherein the cytokine-related condition is allergic inflammation and the antibody inhibits the binding of any one of IL-5, IL-3 or GM-CSF to the IL-5, IL-3 or GM-CSF receptor.

25. (Withdrawn) The method according to claim 23 wherein the allergic inflammation results in asthma.

26. (Withdrawn) The method according to claim 24 wherein the allergic inflammation results in asthma.

27. (Withdrawn) The method according to claim 19 wherein the cytokine-related condition is selected from the group including hemopoiesis, boosting immune response, suppression of embryonic stem cell differentiation, immunostimulation, antitumor activity, expansion of early hemopoietic cells, anemia, correcting thrombocytopenia, wherein said cytokine agonist or antagonist is an agonist.

28. (Withdrawn) The method according to claim 13 wherein the cytokine is selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13; and the presence of an agonist or antagonist is determined by the ability of the agonist or antagonist to activate or inhibit an IL-3, IL-5 GM-CSF, IL-4, or IL-13 response.

29. (Withdrawn) The method according to claim 13 wherein the cytokine agonist or antagonist further binds to Tyr421 or an equivalent residue of a common signaling unit of a cytokine receptor.

30. (Withdrawn) A cytokine agonist or antagonist identified by a method according to claim 13.

31. (Withdrawn) The method according to claim 13 wherein the cytokine is selected from the group consisting of IL-3, IL-5, GM-CSF, IL-4 and IL-13; and the presence of an agonist or antagonist is determined by the ability of the agonist or antagonist to activate or inhibit an IL-3, IL-5, GM-CSF, IL-4, or IL-13 response.

32. (Currently amended) The cytokine-binding domain structure according to claim 1 which comprises a hydrophobic patch, said patch ~~having residues selected from a group consisting of comprising residues~~ Ile338, Ala341, Met361, and Tyr365 of Domain 4 of the β_c chain having a spatial configuration according to Figure 1C and which forms part of a lip at an end of a groove on the surface of the binding domain.

33. (Currently amended) The cytokine-binding domain structure according to claim 31 32 further comprising Met340, and Pro342, and Lys362 of the Domain 4 of a β_c chain.

34. (Currently amended) The cytokine-binding domain structure according to claim 31 32 further comprising Ile368 or Tyr421 of the Domain 4 of a β_c chain.

35. (Canceled)

36. (New) The isolated cytokine binding domain structure according to claim 1 wherein the B'-C' loop comprises residues 362 to 368 of Domain 4 of a β_c chain.

37. (New) The isolated cytokine binding domain structure according to claim 1 wherein the F'-G' loop comprises residues 416 to 422 of Domain 4 of a β_c chain.

38. (New) The isolated cytokine binding domain structure according to claim 1 wherein the B'-C' loop comprises residues Tyr365, His367, Ile368 of D4 β_c which form a cytokine binding triad that converges to form a pivot point.

39. (New) The cytokine binding domain structure according to claim 1 wherein the type 1 β -turn is formed from residues 365 to 368 of Domain 4 of a β_c chain.

40. (New) The cytokine binding domain structure according to claim 11 wherein the type IV β -turn comprises Arg418 and Tyr421 which Tyr421 projects away from the structure according to Figure 1A.